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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/733,239	BLAKE ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/04/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28 and 48-50* is/are pending in the application.

4a) Of the above claim(s) *14-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 48-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 29-47 are cancelled. Claim 50 is added. Claims 1-28 and 48-50 are pending. Claims 14-28 are withdrawn from consideration as being directed to a non-elected invention. Claims 1-13 and 48-49 are under examination.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-3, 7-9 and 48-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cosand,[1] in view of Rosen et al.[2] and Storey et al.[3]

In response to the rejection, Applicant submits the Coleman declaration under 37 C.F.R. § 1.132, together with Coleman's curriculum vitae. Applicant submits that the Coleman declaration sets forth that the references do not provide sufficient motivation to the skilled artisan to achieve the claimed invention, and that non-obviousness is further shown by commercial success of peptides according to the present invention.

In assessing the weight to be given expert testimony, the examiner may properly consider, among other things, 1) the nature of the fact sought to be established, 2) the

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[1] Cosand et al. U.S. Patent No. 4629783, published December 16, 1986.
[2] Rosen et al. WO 87/06005, published October 08, 1987.
[3] Storey et al. Studies on polypeptides. LI. Application of S-ethylcarabmoylcysteine to the synthesis of a protected heptatetracontapeptide related to the primary sequence of ribonuclease T_1. Journal of the American Chemical Society, August 23, 1972, Vol. 94, No. 17, 6170-6178.

strength of any opposing evidence, 3) the interest of the expert in the outcome of the case, and 4) the presence or absence of factual support for the expert's opinion. See Ex parte Simpson, 61 USPQ2d 1009 (BPAI 2001), Cf. Redac Int'l. Ltd. v. Lotus Development Corp., 81 F.3d 1576, 38 USPQ2d 1665 (Fed. Cir. 1996), Paragon Podiatry Lab., Inc. v. KLM Lab., Inc., 948 F.2d 1182, 25 USPQ2d 1561, (Fed. Cir. 1993). The first fact to be sought is whether the claimed invention has commercial success. The Coleman declaration, which is written by a co-inventor of the claimed invention, has been carefully considered, however, it is found that the claim of commercial success is not sufficient to overcome the rejection because the commercial success claim is not commensurate in scope with the claimed invention. The full breadth of the claimed invention encompasses all peptides that comprises 6-50 amino acids, two Cys residues that are separated from each other by at least two but fewer than twenty non-Cys amino acid residues, wherein the thiol groups of the Cys residues are reversibly protected from oxidation by a chemically reversible means resistant to high acidic cleavage conditions used for peptide cleavage from the synthesis solid support, and the most limiting breadth of the claims encompass a peptide having at least seven continuous amino acids with in SED ID NO: 1. However, in the commercial success claimed by Applicant, Applicant has not clearly set forth that **a representative number** of the peptides encompassed by the claims have commercial success. All that Applicant has provided is generic language directing the presence of a peptide, that reads on a scope of the peptides recited in the claims, that has commercial success. That is, Applicant asserted that the peptide used in both the Rapid Test and Peptide EIA

test is a peptide that comprises 6-50 amino acids, two Cys residues that are separated from each other by at least two but fewer than twenty non-Cys amino acid residues, wherein the thiol groups of the Cys residues are reversibly protected from oxidation by a chemically reversible means resistant to high acidic cleavage conditions used for peptide cleavage from the synthesis solid support. To overcome this rejection, Applicant must show commercial success that is commensurate in scope with the claimed invention.

Additionally, the othher fact to be established is whether the claimed invention is obvious over the combined teachings of Cosand, in view of Rosen et al. and Storey et al. The Coleman declaration includes assertions that the references do not provide sufficient motivation to the skilled artisan to achieve the claimed invention because they do not teach or suggest the claimed invention's solution to a technical problem in the immunoassay art nor do the references teach the claimed invention. While these assertions has been considered, however it is not found persuasive. Applicant is reminded that the claimed invention is directed at a composition, not an immunoassay or a method of using the claimed composition to overcome the technical problem in the immunoassay art. Regardless of how the claimed composition is intended to the used, the patentability determination for the claimed invention is solely limited to the composition itself.

In addition to above, it is noted that Applicant further submits that Cosand, Rosen et al. and Storey et al., individually, does not provide any clear and particular motivation to modify their individual teachings to arrive at the claimed invention. In response to

applicant's arguments against the references individually, it should be noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or **in the knowledge generally available to one of ordinary skill in the art**. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation and suggestion to modify the peptides of Cosand is provided by the knowledge generally available to one of ordinary skill in the art, as accorded by Rosen et al. and Storey et al., at the time the invention was made.

Applicant further notes that Applicant submits that Rosen et al. teaches away from the claimed invention. Specifically, Applicant asserts that Rosen teaches away from the claimed invention by teaching that polymeric oxidative forms are advantageous over cyclic, monomeric forms, and cited lines 27-31, page 22 of Rosen et al.

This submission has been considered, however, it is not found persuasive. The cited passage directs a comparison between cyclic monomer forms and polymer forms. The cited passage is not directed at a comparison between noncyclic monomers, as claimed, and polymer forms. It appears that Applicant has inadvertently misconstrued the cited teachings of Rosen et al. In the instant case, Rosen et al. establishes that

oxidative forms of a peptide have a role in affecting or influencing the results of immunoassays.

As previously presented, the claims are directed to a composition comprising an isolated peptide, wherein the peptide is immobilized on a solid phase support following the synthesis and cleavage of the peptide from a synthesis solid support, comprises at least one epitope that is capable of binding to antibodies; and comprises an amino acid sequence of 6 to 50 amino acids, wherein the sequence comprises two Cys residues that are separated from one another by at least 2 but fewer than 20 non-Cys amino acid residues, and wherein the thiol groups of the Cys residues are reversibly protected from oxidation by a chemically reversible means that is resistant to the highly acidic condition used during cleavage of the peptide from its synthesis solid support.

Claim 2, which depends on claim 1, requires the thiol groups be protected from oxidation by ethylcarbamoyl, acetamidolmethyl; 3-nitro-2-pyridinesulfinyl or diphenyl-4-pyridylmethyl. Claim 3, which depends on claim 2, requires the thiol groups be protected from oxidation by ethylcarbamoyl. Claim 7, which depends on claim 1, requires the Cys residues be separated by one another by 4 to 6 non-Cys residues.

Claim 8, which depends on claim 1, requires the peptide to be capable of binding to antibodies to a retroviral transmembrane protein. Claim 9, which depends on claim 8, defines the retroviral protein as an HIV-1 gp41, and requires the peptide to comprise at least seven contiguous amino acids within SEQ ID NO: 1.

Claim 48, which depends on claim 1, requires the highly acidic cleavage condition to comprise hydrofluoric acid (HF) or trifluoroacetic acid (TFA). Lastly, claim

49, which depends on claim 1, requires the solid phase to be a microtiter, a glass bead, a latex bead entrapped on a microporous membrane, a tube, a filter or a chromatographic surface.

Cosand teaches several peptides that are capable of binding to antibodies. One of the peptide that Cosand teaches is a peptide V. Peptide V has the following sequence: Arg-Ile-Leu-Ala-Val-Glu-Arg-Tyr-Leu-Lys-Asp-Gln-Gln-Leu-Leu-Gly-Ile-Trp-Gly-Cys-Ser-Gly-Lys-Leu-Ile-Cys. [Lines 30-40, column 5.] Peptide V has 26 amino acid residues in length. Thus, Peptide V does comprise an amino acid sequence of 6 to 50 amino acids. Peptide V comprises two Cys residues that are separated from one another by 5 non-Cys residues. Thus, Peptide V comprises two Cys residues that are separated from one another by at least 2 but fewer than 20 non-Cys amino acid residues, and Cys residues that are separated by one another by 4 to 6 non-Cys residues. Peptide V is amidated at the C-terminus. Additionally, peptide V is 100% identical to the amino acid sequence set forth in SEQ ID NO: 1. Peptide V comprises the 26 amino acid residues that correspond to a part of the HIV gp41 protein.

Cosand also teaches immobilizing the peptides to the solid phase support following the synthesis of the peptide from a synthesis solid support. The solid phase support used by Cosand includes chromatographic surfaces and microtiter plates. [Column 10, and Tables 1-3.]

The difference between the claimed invention is: The thiol group present in the peptide of Cosand is not reversibly protected from oxidation by a chemically reversible means, including ethylcarbamoyl, that is resistant to the highly acidic condition used

during cleavage of the peptide from its synthesis solid support. It should be noted that the highly acidic condition used by Cosand during cleavage of the peptides comprises hydrofluoric acid (HF). [Lines 7-15 of column 10.]

However, Rosen et al. teaches that peptides that possess more than two cysteine residues may form cyclic monomers, linear or cyclic dimers, and linear polymers of various lengths due to the reduction of the thiol group present on cysteine residues by oxidation. [Lines 15-30 of page 10] Rosen et al. further notes that the cyclic monomer of the peptides is believed to be less efficient in binding to the microtiter wells, and is less suited as a solid phase component of the Enzyme-Linked Immunosorbent Assay (ELISA), which Rosen et al. used to detect for the presence of HIV related antibodies. [Lines 27-35 of page 22]

And Storey et al. teaches the use of ethylcarbamoyl to reversibly protect cysteine residues from oxidation. Specifically, Storey et al. uses ethylcarbamoyl to protect cysteine from the highly acidic highly acidic condition used during cleavage of the peptide from its synthesis solid support. Storey et al. notes that ethylcarbamoyl is stable toward strong acid. [Sulfhydryl Protection section, page 6171.] Hence, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use ethylcarbamoyl to reversibly protect cysteine from oxidation. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to control the oxidative form of peptides comprising more than one cysteine residue, and to provide a suitable solid phase component of the Enzyme-Linked Immunosorbent Assay (ELISA). One of ordinary skill in the art at the time the invention

was made would have had a reasonable expectation of success for doing so because the use of ethylcarbamoyl to protect cysteine from the highly acidic condition used during cleavage of the peptide from its synthesis solid support is routinely practiced in the art.

4. Claims 1, 4-6, 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cosand, in view of Rosen et al. and Storey et al., as applied to claims 1 and 8-9, in further view of Cosand et al.[4]

In response to the rejection, Applicant submits the Coleman declaration under 37 C.F.R. § 1.132, together with Coleman's curriculum vitae. Applicant submits that the Coleman declaration sets forth that the references do not provide sufficient motivation to the skilled artisan to achieve the claimed invention, and that non-obviousness is further shown by commercial success of peptides according to the present invention.

The Coleman declaration is discussed above.

Additionally, it is noted that Applicant submits that Cosand et al. does not remedy the deficiencies of the Cosand, Rosen et al. and Storey et al. Specifically, Applicant submits that Cosand et al. does not provide any clear or particular motivation to modify the peptide of Cosand to achieve the claimed invention.

Applicant's submission has been considered, however, it is not found persuasive. Applicant is reminded that the rejection over Cosand in view of Rosen et al. and Storey et al., as applied to claims 1 and 8-9, in further view of Cosand et al. and not just between Cosand and Cosand et al. Additionally, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that

obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the difference between the claimed invention and the combined teachings of Cosand, Rosen et al. and Storey et al. is: the peptide of Cosand is not modified at the N-terminus with a third cytosine or the sequence Cys-Gly-Gly. However, Cosand does suggest modifying the peptide with the addition of other amino acids including cytosine at the C or N-terminus of the peptide to provide a useful functionality for linking the peptide to a support or other peptides. [Lines 60-68 of column 3 to lines 1-2 of column 4] Furthermore, Cosand et al. teaches the use of cysteine in combination of other intervening amino acid spacers. [Paragraph bridging columns 3-4.] Additionally, Cosand et al. encourages the use of one to three glycine residues as preferred amino acid spacer to facilitate coupling between the peptide and a support or other peptides. Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to add a third cysteine and one to three glycine residues to the N-terminus of a peptide. One of ordinary skill in the art at the time the invention was made would have been motivated to facilitate the coupling of the peptide to a support or other peptides. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because modification of peptide with amino acid linkers is well practiced in the art.

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[4] Cosand et al. U.S. Patent No. 5075211, filed November 14, 1986.

As previously presented, claim 4, which depends on claim 1, requires the peptide to comprise a third Cys residue at the N-terminus of the peptide, wherein the third Cys residue is not protected from oxidation. Claim 5, which depends on claim 4, specifies that the sequence Cys-Gly-Gly be at the N-terminus of the peptide. Claim 6, which depends on claim 4, requires the C-terminus of the peptide be amidated.

Claim 10, which depends on claim 9, requires the N-terminus of the peptide to comprise additional amino acids to enhance specific binding of the antibodies to the protein, and wherein at least one of the additionally amino acids is a third Cys residue, wherein the third Cys residue is not protected from oxidation. Claim 11, which further limits claim 10, requires the third Cys residue be the N-terminal residue of the peptide. Claim 12, which depends on claim 11, specifies that the sequence Cys-Gly-Gly be at the N-terminus of the peptide. Lastly, claim 13, which depends on claim 11, requires the C-terminus of the peptide be amidated.

The significance of Cosand, Rosen et al. and Storey et al., as it pertains to claims 1 and 8-9 is provided above. As summarized above, Cosand teaches a peptide is amidated at the C-terminus.

The difference between the claimed invention and the teachings of Cosand, Rosen et al. and Storey et al. is: the peptide of Cosand is not modified at the N-terminus with a third cytosine or the sequence Cys-Gly-Gly. However, Cosand does suggest modifying the peptide with the addition of other amino acids including cytosine at the C or N-terminus of the peptide to provide a useful functionality for linking the peptide to a support or other peptides. [Lines 60-68 of column 3 to lines 1-2 of column 4]

Furthermore, in U.S. Patent No. 5075211, Cosand et al. teaches the use of cysteine in combination of other intervening amino acid spacers. [Paragraph bridging columns 3-4.] Additionally, Cosand et al. encourages the use of one to three glycine residues as preferred amino acid spacer to facilitate coupling between the peptide and a support or other peptides. Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to add a third cysteine and one to three glycine residues to the N-terminus of a peptide. One of ordinary skill in the art at the time the invention was made would have been motivated to facilitate the coupling of the peptide to a support or other peptides. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because modification of peptide with amino acid linkers is well practiced in the art.

5. Claims 1 and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cosand, in view of Rosen et al. and Storey et al., as applied to claims 1 and 8-9, in further view of Marshall.[5]

Claim 50, which depends on claim 49, limits the solid phase to latex beads, and requires the bead to be entrapped in a microporous membrane.

The significance of Cosand, Rosen et al. and Storey et al., as it pertains to claims 1 and 49 is provided above. Cosand, Rosen et al. and Storey et al. do not teach the limitation of claim 50. However, Cosand does suggest the use of his peptides to detect AIDS-related diseases, including HIV.

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[5] Marshall, U.S. Patent Application No. 07/877862, filed May 04, 1992, published as U.S. Patent No. 5501949.

At the time the invention was made, Marshall a solid phase system for detecting and quantifying an analyte suspected of being in a specimen, wherein the analyte is a compound or an organism suspected in the specimen sample. [Lines 20-25, column 1 and lines 65-67, column 3, in particular.] The system of Marshall includes a solid phase that is latex beads. Marshall teaches the use of the latex beads to immobilize peptides. Marshall then teaches the entrapment of the latex beads with the immobilized peptides in a microporous membrane. [Columns 4-6, in particular.] Marshall teaches that this solid phase system overcomes the problems noted in the art, which includes the need for a solid phase that would be compatible with an easy-to-use separation system, that provided accurate and repeatable results, and a solid phase that permits a rapid equilibrium to be established between antibody and antigen so as to promote rapid binding of the two. [Lines 5-22, column 3, in particular.]

Hence, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to use the peptides of Cosand with the solid phase system of Marshall. One of ordinary skill in the art, at the time the invention was made would have been motivated to do so to detect HIV. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because Marshall teaches solid phase system for detecting and quantifying an analyte suspected of being in a specimen.

Conclusion

6. No claims are allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bruce R. Campell/
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